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Uncomplicated Male Gonorrhea—A Review

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VENEREAL DISEASE is California's major communicable disease (Table 1) and gonorrhea is the leading reportable disease for 1971 (Table 2). The reported cases of gonorrhea in California and the United States have continued to increase at a high rate, but a slight decline has been recorded for California in 1971 (Table 3). However, adding unreported cases throughout the United States to those reported by physicians, one finds the estimated incidence of gonorrhea is approximately two million cases per year.[1] In 1970, a survey was conducted by the National Disease and Therapeutic Index of a representative sample of more than 1,500 private physicians. The findings were startling. Patients with gonococcal infections represented more than half of all venereal disease visits during 1970. Patient visits were mostly by males, 69 percent.[2] Thus, an epidemic of gonorrhea prevails.

Signs and Symptoms

The gonococcus, in the majority of cases, gains entry into the body by way of the genital tract. Less frequent sites of initial infections are the conjunctivas and rectal mucosa. The type of mucosa found in a particular part of the genitourinary tract basically determines the susceptibility of that tissue to gonococcal infection. Stratified squamous epithelium, which covers the external genitalia, extends for approximately 2 cm into the male urethra and is not susceptible to infection. Columnar epithelium, which lines the anterior urethra, urethra glands, prostatic ducts and prostate, seminal vesicles, vas deferens and epididymis, furnishes fertile soil for growth of the gonococcus. Transitional epithelium which lines the posterior urethra and the bladder is also susceptible to invasion by gonococci.[3]

Following the gonococcal infection of the genital tract, the incubation period is usually two to eight days, and the average is from three to five days. (However, the incubation period may be quite long, and several weeks can elapse before the patient notices any symptoms).

The initial symptom of gonorrhea in males is most often acute anterior urethritis, manifested

TABLE 1.—*California's Major Communicable Diseases, 1971*

	Reported Cases
Venereal Disease	114,000
Streptococcal infection	31,000
Hepatitis	11,000
Mumps	8,000
Rubella	8,000
Tuberculosis	4,000

Source: "California Morbidity," 1/7/72. California State Department of Public Health.

TABLE 2.—*California's Leading Reportable Diseases, 1971*

	Reported Cases
Gonorrhea	102,000
Streptococcal infection	31,000
Syphilis	12,000
Hepatitis	11,000
Mumps	8,000
Rubella	8,000
Tuberculosis	4,000

Source: "California Morbidity," 1/7/72. California State Department of Public Health.

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TABLE 3.—*Trends in Reported Civilian Cases and Rates of Gonorrhea per 100,000 Population*

United States and California, Fiscal Years 1968-1971

	1968		1969		1970		1971	
	Cases	*Rate*	*Cases*	*Rate*	*Cases*	*Rate*	*Cases*	*Rate*
United States*	431,380	219.2	494,227	245.9	600,072	292.7	624,371	304.6
California**	76,020	380.1	90,029	453.4	103,429	517.5	101,650	509.4

Source: *U.S. Public Health Service
**California State Department of Public Health

by a purulent urethral discharge and burning on urination. The discharge is most commonly yellow or brown; the meatus is red and edematous; and the urethra may be thickened and tender. Frequency, urgency and nocturia do not occur unless the posterior urethra and prostate gland become involved.

Acute prostatitis with the accompanying involvement of the seminal vesicles will cause fever, urinary symptoms, and frequently pain as well, generally deep-seated in the perineal region but often noted in the suprapubic or inguinal area or even in the sacral and lower lumbar areas.

An even more distressing involvement is that of acute epedidymitis. This is marked by pain in the scrotum (frequently wrongly attributed at first to orchitis or torsion) swelling and fever. With some exceptions this complication is associated with prostatitis as well.

Diagnosis

The presence of Gram-negative intracellular diplococci in a smear of the urethral exudate of a male patient, associated with typical clinical symptoms, is virtually diagnostic. If the smear examination does not reveal the organism, culture specimens must then be taken from the anterior urethra and inoculated on Thayer-Martin selective medium for laboratory cultivation.[4] The combination of a positive oxidase reaction of colonies and Gram-negative diplococci grown in the medium provides sufficient criteria for a diagnosis of gonorrhea. In homosexuals, a culture specimen should be taken from the anal canal and pharynx.[5]

The sending of urethral specimens taken in a private physician's office or a clinic to a distant laboratory has now been improved by the development of a new transport medium, Transgrow®, which is a modified Thayer-Martin antibiotic selective medium.[6] Transgrow medium is in an atmosphere of 10 percent carbon dioxide and 90 percent air; the medium is further enriched by increasing the agar content to 2 percent and the dextrose content to 0.25 percent.

It is well for the physician to keep in mind that gonorrhea may go unrecognized. Subacute or completely asymptomatic infections have evaded detection. Asymptomatic gonorrhea in males has been further substantiated by recent studies of Thatcher, et al.[7]

Gonococcal urethritis in men must be distinguished from nonspecific urethritis, which is not a single disease entity but a symptom of many diseases, including those caused by the mycoplasma organisms.[8] With mycoplasma urethritis, which may or may not be associated with intercourse, the incubation period is highly variable and usually prolonged. The urethral discharge tends to be scant, white and mucoid. On smear, miscellaneous organisms are present, while on culture there is no growth of Neisseria gonorrhoeae. The response to treatment is rather disappointing.

Therapy

Aqueous procaine penicillin G, 2.4 million units, intramuscularly, in one session, has been the treatment of choice in male gonococcal urethritis. This has been reiterated in studies performed by the Alameda County Health Care Services Agency,[9,10] including cooperative clinic studies conducted in venereal disease clinics throughout the United States.[11] However, with the increased resistance of the gonococci, the United States Public Health Service is now recommending that 4.8 million units of aqueous procaine penicillin G be given intramuscularly, in one session, preceded by one gram of probenicid by mouth, preferably at least 30 minutes before the injection.[12]

Over the years, Neisseria gonorrhoeae has

become increasingly resistant to penicillin.[13-15] However, this resistance is relative, not absolute. Studies of Cave and associates[16] further substantiated this; they found that a high proportion of strains were relatively resistant to penicillin G, but none of the strains were absolutely resistant. Similar findings have been reported in Europe.[17]

Recently, the Center for Disease Control, United States Public Health Service, released its latest findings concerning the bi-annual penicillin susceptibility testing program of gonococcal isolates.[18] The 2,117 cultures studied before 1971 indicated a trend toward increased resistance to penicillin. However, "preliminary data from susceptibility testing of 739 cultures isolated during 1971 suggest the upward trend in penicillin resistance may be leveling off."

Therefore, currently, most gonococci are still sensitive to the levels of penicillin achieved by one dose therapy. But it must be emphasized that the antibiotic must be given in adequate dosage, and at the same time it should be stressed that suboptimal doses must not be used.

Alternative Therapy

Tetracycline is an acceptable alternate antibiotic if the patient has allergic reaction to penicillin or the organism is resistant to it.[19,20] Treatment regimen in males is an initial oral dose of 1.5 grams followed by 0.5 gram orally every four to six hours for a total of 9 grams. (A recent study in our clinic, not yet published, has established a 95 percent cure rate in men receiving an initial oral dose of 2.0 grams of tetracycline hydrochloride and followed by 0.5 gram every four to six hours for a total of 7.5 grams). Doxycycline and ampicillin are also effective in recommended dosages.[21,22] (Of course, ampicillin cannot be utilized for the penicillin-allergic patient). However, increased resistance to these antibiotics as well as to tetracycline is a matter of continuing concern. Furthermore, strains relatively resistant to penicillin also tend to have diminished susceptibility to these other drugs.[23,24]

Excellent results have been obtained by combining procaine penicillin G, 2.4 million units, with the administration of 1.0 gram of probenecid given orally one hour before the injection. Similar results have also been reported with ampicillin sodium, 2 grams, preceded by 1.0 gram of probenecid given orally one hour before injection.[25] (The use of probenecid inhibits the excretion of penicillin and ampicillin; therefore, the antibiotic reaches higher serum levels which are maintained for a long period).

A new drug, spectinomycin hydrochloride, has recently been licensed in the United States for treatment of only gonorrhea. A 2.0 gram intramuscular injection, in one session, has proven most effective in males.[26,27] However, it must be kept in mind that spectinomycin is recommended as an alternate antibiotic to penicillin, not as the drug of choice, for male gonorrhea.

Follow-Up

The importance of follow-up examination needs to be stressed to the patient. A test of cure should be routine. Follow-up cultures are essential for the immediate detection of treatment failure, since we know that symptoms may be completely suppressed by suboptimal therapy.

At times it is difficult to distingiush between treatment failure and reinfection, for the incubation period is short and effective immunity is lacking. Clinical symptoms at follow-up two to five days following therapy may be due not to treatment failure but to reinfection, especially if the patient has had sexual re-exposure to his untreated sex contact ("ping-pong" disease). Retreatment generally consists of doubling the initial therapeutic dose, in one session.

Concurrent Syphilis

The gonorrhea patient should also be assessed for syphilis, including a serologic test, for it is possible for both diseases to be present in the same patient. If infectious syphilis is diagnosed, either on the basis of a reactive serologic test or a lesion positive on darkfield examination, the standard treatment for syphilis must be given simultaneously with the treatment for gonorrhea.

A recent study by the United States Public Health Service[28] indicates that aqueous procaine penicillin G in doses of 2.4 or 4.8 million units, intramuscularly in one session, is effective therapy for *incubating* syphilis. Therefore, the investigators point out, "Patients with gonorrhea who have been named as contacts of persons with infectious syphilis and are treated with these schedules do not need additional therapy with penicillin G benzathine. It should be emphasized that such patients should receive a thorough

physical examination, including darkfield examination of all suspicious lesions and serologic tests to rule out syphilis before gonorrhea therapy is instituted . . ." These results permit a modification of the long recommended practice of following gonorrhea patients with three monthly serologic tests for syphilis. Furthermore, patients with confirmed gonococcal urethritis who have been treated with 2.4 or 4.8 million units of aqueous procaine penicillin G, intramuscularly in one session, also no longer need to be followed with serologic tests.

A word of caution about tetracyclines: Tetracycline may be effective in syphilis if it is administered over a prolonged period and in adequate dosage. However, the short treatment schedule prescribed in gonorrhea is not adequate to abort all cases of incubating syphilis; hence, gonorrhea patients treated with tetracycline must continue to receive adequate serologic follow-up.

Summary

Although the clinical signs and symptoms of gonorrhea in males are usually specific and somewhat pathognomonic in uncomplicated cases, definitive diagnosis can only be based on a Gram-stain smear; subsequent cultures are also indicated in some cases.

The drug of choice is still intramuscular aqueous procaine penicillin G. Although penicillin resistance is well established, this is relative and not absolute. Follow-up examinations should be routine on all patients. Cultures provide an immediate detection of all therapeutic failures. Retreatment, of course, is mandatory to prevent the spread of resistant strains.

In all instances of gonorrhea in males, the possibility of concurrent syphilis must be considered. Current research indicates that the use of procaine penicillin G eliminates *incubating* syphilis as well, which reinforces the case for penicillin as the drug of choice.

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